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論　文　題　名　Regulatory mechanism of CCN2 production by serotonin (5-HT) via 5-HT$_{2A}$ and 5-HT$_{2B}$ receptors in chondrocytes.
（軟骨細胞における 5-HT2A および 5-HT2B 受容体を介したセロトニン（5-HT）による CCN2 産生の調節機構）

論文内容の要旨（2000字程度）

Serotonin (5-hydroxytryptamine: 5-HT) is recognized as a neurotransmitter in the central nerve system and as a regulator of systemic blood pressure in the peripheral tissues. Recently, it was reported that 5-HT2 receptors (5-HT2Rs) were expressed in cartilage tissues lacking both vessels and neurons, suggesting possible novel functions of 5-HT during cartilage development and regeneration. Our previous data indicated that CCN family protein 2/connective tissue growth factor (CCN2/CTGF) plays a central role in cartilage development and regeneration. Therefore, the aim of this study was to investigate the effect of 5-HT on the production of CCN2 in chondrocytes. Firstly, we showed that the mRNAs of 5-HT2R subtypes 5-HT2AR and 5-HT2BR, were expressed in a human chondrocytic cell line, HCS-2/8; however, 5-HT2CR mRNA was not detected. In addition, exogenously added 5-HT did not affect the 5-HT2AR and 5-HT2BR expressions. Next, we demonstrated that CCN2 production was increased by treatment with a 5-HT2AR agonist and the combination of 5-HT and 5-HT2BR antagonist. In contrast, treatment with a 5-HT2BR agonist and the combination of 5-HT and 5-HT2AR antagonist decreased CCN2 production. Furthermore, we showed that phosphorylation of Akt and p38 MAPK were increased by treatment with 5-HT2AR agonist, and that phosphorylation of PKCε, PKCζ, ERK1/2 and JNK were increased by treatment with 5-HT2BR agonist. Finally, we found that 5-HT2AR was localized in the growth plate, whereas 5-HT2BR was localized in the articular cartilage.

論文内容の要旨（2000 字程度）

These findings suggest that 5-HT promotes CCN2 production through the 5-HT2AR in growth plates, and that it represses CCN2 production through the 5-HT2BR in articular cartilage for harmonized development of long bones.